

PATENT COOPERATION TREATY
PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference N. 70330D	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/GB 96/02960	International filing date (<i>day/month/year</i>) 29/11/1996	(Earliest) Priority Date (<i>day/month/year</i>) 29/11/1995
Applicant THE ANTHONY NOLAN BONE MARROW TRUST et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.
 It is also accompanied by a copy of each prior art document cited in this report.

1. Certain claims were found unsearchable (see Box I).
2. Unity of invention is lacking (see Box II).
3. The international application contains disclosure of a nucleotide and/or amino acid sequence listing and the international search was carried out on the basis of the sequence listing
 - filed with the international application.
 - furnished by the applicant separately from the international application,
 - but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
 - Transcribed by this Authority
4. With regard to the title,
 - the text is approved as submitted by the applicant.
 - the text has been established by this Authority to read as follows:
5. With regard to the abstract,
 - the text is approved as submitted by the applicant.
 - the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.
6. The figure of the drawings to be published with the abstract is:
 Figure No. _____
 - as suggested by the applicant.
 - because the applicant failed to suggest a figure.
 - because this figure better characterizes the invention.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 96/02960A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95 01453 A (UNIV LELAND STANFORD JUNIOR ;US HEALTH (US)) 12 January 1995 see abstract see page 6 - page 7	1
Y	WO 95 07345 A (CHUNG YEON BO) 16 March 1995 see abstract; claim 1	2-38
X	US 5 468 611 A (BAXTER-LOWE LEE A ET AL) 21 November 1995	1
Y	see column 3, line 35 - line 50 see column 27, line 4 - line 5; example	2-38
A	EP 0 575 845 A (HOFFMANN LA ROCHE) 29 December 1993	

	-/-	

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

21 April 1997

07. 05. 97

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl,
Fax (+ 31-70) 340-3016

Authorized officer

Ceder, O

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 96/02960

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	NUCLEIC ACIDS RESEARCH, vol. 23, no. 24, 1995, pages 5082-5084, XP000606029 BABON J J ET AL: "IMPROVED STRATEGY FOR MUTATION DETECTION--A MODIFICATION TO THE ENZYME MISMATCH CLEAVAGE METHOD" --- A NUCLEIC ACIDS RESEARCH, vol. 17, no. 17, 1989, pages 6821-6840, XP000670253 BHATTACHARYYA ET AL: "The contrasting structures of mismatched DNA sequences containing looped-out bases" cited in the application -----	
1		

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 96/02960

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9501453 A	12-01-95	NONE		
WO 9507345 A	16-03-95	NONE		
US 5468611 A	21-11-95	US 5545526 A		13-08-96
EP 0575845 A	29-12-93	AU 675431 B		06-02-97
		AU 4142293 A		06-01-94
		CA 2098947 A		24-12-93
		JP 6078800 A		22-03-94
		NZ 247935 A		28-08-95

INTERNATIONAL SEARCH REPORT

Information application No

PCT/GB 96/02960

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12Q

1998

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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Y	WO 95 07345 A (CHUNG YEON BO) 16 March 1995 see abstract; claim 1	2-38
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- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

1

Date of the actual completion of the international search

21 April 1997

Date of mailing of the international search report

07.05.97

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2

Authorized officer

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/GB 96/02960

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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WO 9507345 A	16-03-95	NONE	
US 5468611 A	21-11-95	US 5545526 A	13-08-96
EP 0575845 A	29-12-93	AU 675431 B AU 4142293 A CA 2098947 A JP 6078800 A NZ 247935 A	06-02-97 06-01-94 24-12-93 22-03-94 28-08-95

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PATENT COOPERATION TREATY

REC'D 03 MAR 1998

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference N.70330D	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (PCT/IPEA/416)
International application No. PCT/GB96/02960	International filing date (day/month/year) 29/11/1996	Priority date (day/month/year) 29/11/1995
International Patent Classification (IPC) or national classification and IPC C12Q1/68		
Applicant THE ANTHONY NOLAN BONE MARROW TRUST et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I Basis of the report
- II Priority
- III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV Lack of unity of invention
- V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI Certain documents cited
- VII Certain defects in the international application
- VIII Certain observations on the international application

Date of submission of the demand 26/06/1997	Date of completion of this report 27.02.98
Name and mailing address of the IPEA/  European Patent Office D-80298 Munich Tel. (+49-89) 2399-0, Tx: 523656 epmu d Fax: (+49-89) 2399-4465	Authorized officer Luzzatto, E Telephone No. (+49-89) 2399-8169



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB96/02960

I. Basis of the report

1. This report has been drawn on the basis of (substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.):

Description, pages:

1-49 as originally filed

Claims, No.:

1-38 as originally filed

Drawings, sheets:

1/14-14/14 as originally filed

2. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:
- the drawings, sheets

3. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c));

4. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB96/02960

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims 2-9,14,17-25,27,29,31-38
	No:	Claims 1,10-13,15,16,26,28-30
Inventive step (IS)	Yes:	Claims 2-7,18-21,24,25,32-35
	No:	Claims 1,8-17,22,23,26-31,36-38
Industrial applicability (IA)	Yes:	Claims 1-38
	No:	Claims

2. Citations and explanations

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB96/02960

PART V

1) The present application does not meet the requirements of Art. 33(1) and (2) PCT due to lack of novelty over WO-A-9501453 (D1).

D1 (see p. 8, l. 16-32, p. 28, l. 35-p. 29, l. 21, p. 31, l. 27-p. 32, l. 24, p. 39, l. 8-p. 40, l. 32, ex. 7, cl. 19) discloses an assay as that to which independent claims 1 and 29 relate since it comprises the following steps:

a) amplifying the target DNA;

b) denaturing the amplification products;

c) renaturing them in the presence of an excess of a preselected ("reference") DNA molecule and

d) separating the obtained duplexes on a polyacrylamide gel.

It thus anticipates the subject-matter of claims 1, 10-13, 15, 16, 26 and 28-30.

2) The subject-matter of claims 8, 9, 14, 17, 22, 23, 27, 31 and 36-38 relates to features which appear to be commonplace in the art and thus lacks inventive step (Art. 33(1) and (3) PCT).

Concerning claims 17, 22, 23, and 36-38, D1 does not mention HLA or donor-recipient compatibility; it makes it however clear that the method has general applicability to the analysis of sequence diversity, of which HLA analysis is a well known part.

3) On the other hand, the subject-matter of claim 18-21 appears to meet the requirements of Art. 33 PCT since none of the available documents, either alone or in combination, discloses or suggests it.

D1 does not mention the evaluation of genetic compatibility between a potential donor and the recipient as a potential application of the method therein disclosed. In view of the argument put forward above, the skilled person would have thought of applying the method of D1 to the said problem, however he/she would not have had any indication of some of the specific features of the method of claim 18, e.g. the use of an immobilisable primer to separate the "reference" molecules from the starting mixture.

The same applies to document D2 (US-A-5468611), which instead relates explicitly to the problem of donor-recipient compatibility assessment, since it falls short of teaching any heteroduplex formation between the donor and the recipient DNA.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB96/02960

Moreover, no clear-cut indication in the prior art would have led the skilled person to combine these two documents so as to obtain the present invention.

4) The subject-matter of claims 2-7, 24, 25 and 32-35 appears to meet the requirements of Art. 33 PCT.

4.1) As to claims 6 and 7, the use of a primer labelled with a high molecular weight molecule in a method for DNA separation comprising the formation of heteroduplexes with a DNA reference molecule is not disclosed or suggested in the prior art.

4.2) Reasons similar to those given in point 3 above apply also to claims 2-5, 24 and 25.

4.3) Claims 32-35 relate to the use of at least two reference strands: such a feature is not suggested in the prior art and its inventiveness is further supported by the advantages outlined in the description (p. 10-11).

PART VII

To comply with Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1-D2 should be mentioned in the description and these documents should be identified therein.

ENT COOPERATION TREA

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION
(PCT Rule 61.2)

To:

United States Patent and Trademark
Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year)
11 July 1997 (11.07.97)

Applicant's or agent's file reference
N.70330D

International application No.
PCT/GB96/02960

Priority date (day/month/year)
29 November 1995 (29.11.95)

International filing date (day/month/year)
29 November 1996 (29.11.96)

Applicant
ARGUELLO, Rafael et al

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

26 June 1997 (26.06.97)

in a notice effecting later election filed with the International Bureau on:

2. The election was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer
H. Zhou

Telephone No.: (41-22) 338.83.38